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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/855,158	05/14/2001	Lars Eyde Theill	A-686A	8931

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EXAMINER	
CANELLA, KAREN A	
ART UNIT	PAPER NUMBER
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/03/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/855,158	THEILL	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) 13-17 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) 13-15 is/are rejected.

7)☐ Claim(s) 16-17 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 13-17 are pending and under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The rejection of claims 13-15 and under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained for reasons of record. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 13 is drawn to a composition of matter, comprising a formula wherein neither X1 nor X2 is naturally occurring and wherein the X groups comprise P1, P2, P3 and P4, wherein each P is independently selected from the consensus region of TACI, the consensus region of BCMA or the extracellular consensus region of TACI/BCMA, wherein P is not the extracellular region of TACI, or the extracellular region of BCMA and wherein each P is linked via an independently selected linker to an Fc domain, a linear polymer, a branched chain polymer, a lipid, a cholesterol group, a carbohydrate, an oligosaccharide, a natural protein, a synthetic protein or a polypeptide which binds to a salvage receptor. The claims encompass a genus of synthetic molecules which minimally comprise the consensus region of TACI, the consensus region of BCMA or the extracellular consensus sequence of TACI/BCMA. Claims 13-15 do not limit the functional attributes of the encompassed molecules (it is noted that claim 16 specifies that one of P1 and P2 is a specific binding partner for APRIL and the other is a specific binding partner for AGP-3). One of skill in the art would reasonably conclude that claims 13-15 are not limited to binding to AGP-3 or APRIL. Thus, claims 13-15 encompass a genus of molecules which are highly variant because the genus encompasses molecules which differ substantially in structure from the naturally occurring TACI and BCMA because "P" need only comprise the consensus region of TACI and BCMA. The genus of molecules encompassed by claims 13-15 are also highly variant in terms of function because the claims do not require that the molecules bind to the ligands of AGP-3 and/or APRIL. The disclosure of TACI and BCMA as receptors

for AGP-3 and APRIL, and the disclosure that soluble forms of the extracellular portion of the receptor can inhibit binding to the receptor does not adequately describe the claimed genus because the genus encompasses molecules which differ significantly in structure from the extracellular portions of TACI and BCMA as said P groups need only minimally comprise the consensus regions therein thus encompassing other undisclosed proteins which minimally comprise the claimed consensus regions. The disclosure of TACI and BCMA as receptors for AGP-3 and APRIL, and the disclosure that soluble forms of the extracellular portion of the receptor can inhibit binding to the receptor does not adequately describe the claimed genus because the genus encompasses molecules which differ significantly in function from the soluble portion of TACI and/or BCMA because the claims encompass molecules which do not bind to AGP-3 and/or APRIL. One of skill in the art would reasonably conclude that applicant was not in possession of the invention at the time of filing.

Applicant previously argued that the instant invention fulfills the requirements set out by the Written Description Guidelines 66, Fed Reg 1099, 1106 (2001) because the specification explicitly discloses that TACI and BCMA are cell surface receptors for APRIL, APRIL competes with AGP-3 for TACI and BCMA binding, soluble BCMA competes with APRIL and AGP-3 for receptor binding and soluble TACI competes with APRIL and AGP-3 for receptor binding. This has been argued again and considered again but not found persuasive. While the above disclosure was necessary for enablement of the claims, it is not relevant to limiting the functional attributes of the products encompassed by the claims <u>because the claims cannot be read in light of the specification</u>. Applicant argues that the claims must be read in light of the specification, however this is not the same as reading limitations from the specification into the claims. See M.P.E.P.2106

USPTO personnel are to give claims their broadest reasonable interpretation in light of the supporting disclosure. In re Morris, 127 F.3d 1048, 1054-55, 44 USPQ2d 1023, 1027-28 (Fed. Cir. 1997). ***Limitations appearing in the specification but not recited in the claim should not be read into the claim.*** *E-Pass Techs., Inc. v. 3Com Corp., 343 F.3d 1364, 1369, 67 USPQ2d 1947, 1950 (Fed. Cir. 2003) (claims must be interpreted "in*

view of the specification" without importing limitations from the specification into the claims unnecessarily). In re Prater, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-551 (CCPA 1969).

The rejection of claims 13-15 under 35 U.S.C. 103(a) as being unpatentable over Bram et al (WO 98/39361, reference B9 of the IDS filed September 17, 2001) in view of Chaudhary (WO 99/11971, reference B13 of the IDS filed September 17, 2001) is maintained for reasons of record.

Claims 13-15 encompass compositions wherein F1 is a Fc domain, a lipid such as a glycosylphospholipid, or a natural protein such as a transferrin or a hormone or a synthetic protein, and wherein a=1 and b=0 and wherein P is the consensus sequence of TACI with the proviso that X does not comprise a naturally occurring polypeptide.

Bram et al teach chimeric TACI proteins comprising the extracellular domain of a TACI protein linked to the Fc domain of an immunoglobulin a glycosylphospholipid, or a natural protein such as a transferrin, a hormone or a synthetic protein such as the Fv portion of an antibody(page 24, lines 20-34). Bram et al teach synthetic TACI polypeptides comprising a compound of two or more subunit amino acids linked by peptide bonds (page 19, line 33 to page 20, line1). Bram et al teach that TACI comprises two cysteine rich repeats at residues 33-66 and 70-104 which indicate that TACI is a member of the TNF receptor superfamily (page 4, lines 33-34 and page 19, lines 20-31). Bram et al teach a blocking reagent comprising a recombinant form of the extracellular portion of the TACI receptor which acts to intercept the normal endogenous ligands that crosslink and activate the TACI protein (page 8, lines 1-4). Bram et al do not specifically teach the composition comprising a fragment of the extracellular domain of TACI wherein said composition comprises the TACI consensus sequence but does not comprise the entirety of said extracellular domain.

Chaudhary teaches cysteine-rich pseudo repeats in the extracellular domain of the TNF receptor family, wherein said cysteine rich repeats are involved in ligand binding (page 7, lines 24-29).

It would have been prima facie obvious at the time the claimed invention was made to substitute a polypeptide comprising residues 33-104 for the complete extracellular domain in the

fusion proteins as taught by Bram et al , and also to make a synthetic polypeptide as taught by Bram et al comprising a cysteine repeat region as a "subunit amino acids" linked by peptide bonds. One of skill in the art would have been motivated to do so by the teachings of Bram et al on the recombinant form of TACI comprising the extracellular portion of TACI which acts to intercept the endogenous ligands of TACI and the teachings of Chaudhary which identify the cysteine repeat regions of members of the TNF-receptor family as important for ligand binding. One of skill in the art would expect that a polypeptide which is shorter than the complete extracellular domain of TACI would be able to intercept exogenous ligands which activate the native TACI receptor as long as said polypeptide comprised the cysteine rich regions identified by Chaudhary as important in ligand binding.

The rejection of claims 13-15 under 35 U.S.C. 103(a) as being unpatentable over Shu (U.S. 6,475,987) in view of Chaudhary (WO 99/11971, reference B13 of the IDS filed September 17, 2001) is maintained for reasons of record.

Claims 13-15 encompass compositions wherein F1 is a Fc domain, and wherein a=1 and b=0 and wherein P is the consensus sequence of BCMA, wherein X does not comprise a naturally occurring polypeptide.

Shu teaches that BCMA is a member of the TNF receptor family and that BCMA is the receptor for TALL-1 (column 9, lines 18-43). Shu teaches a method for identifying compounds that regulate the interaction between TALL-1 and its receptor (BCMA) comprising determining whether a putative regulatory compound affects the binding of TALL-1 to the receptor (BCMA) (column 7, lines 3-27). Shu teaches that fusion proteins comprising one or more extracellular domains of BCMA can be used in a non-cell based screening assay to identify compounds for the ability to bind to BCMA (column 38, lines 31-35 and 42-46). Shu teaches a composition comprising the extracellular domain of BCMA fused to the Fc domain of an immunoglobulin (column 46, lines 14-18).

Chaudhary teaches cysteine-rich pseudo repeats in the extracellular domain of the TNF receptor family, wherein said cysteine rich repeats are involved in ligand binding (page 7, lines 24-29).

It would have been prima facie obvious at the time the claimed invention was made to substitute a polypeptide comprising the cysteine rich repeats of BCMA for the one or two extracellular domains of BCMA in a fusion protein comprising the immunoglobulin Fc domain as taught by Shu. One of skill in the art would have been motivated to do so by the teachings of Chaudhary which identify the cysteine repeat regions of members of the TNF-receptor family as important for ligand binding. One of skill in the art would expect that a polypeptide which is shorter than the complete extracellular domain of BCMA would function in a assay to identify compounds which bind to the extracellular portion of BCMA

Applicant again argues that the disclosure of Chaudhary regarding the involvement of the cysteine-rich pseudo repeats with ligand binding to a TNF receptor do not provide motivation to combine the references because "involvement" cannot be interpreted as necessary and sufficient for ligand binding. Applicant states that the disclosure of the '791 publication teaches against the instant invention as it clearly only contemplates the use of the entire extracellular domain. This has again been considered and found not to be persuasive.

1. Shu teaches that BCMA is a member of the TNF receptor family.
2. Bram et al teach that TACI comprises two cysteine rich repeats at residues 33-66 and 70-104 which indicate that TACI is a member of the TNF receptor superfamily (page 4, lines 33-34 and page 19, lines 20-31).C
3. Chaudhary teaches cysteine-rich pseudo repeats in the extracellular domain of the TNF receptor family, wherein said cysteine rich repeats are involved in ligand binding.

Therefore there is a reasonable expectation of success that the cysteine-rich pseudo repeats in BCMA and TACI are involved in ligand binding. One of skill in the art need only have a reasonable expectation of success to be motivated to combine the references on the basis of the teachings of Chaudhary et al Applicant is referred to section 2143.02 the MPEP, wherein it is stated

OBVIOUSNESS REQUIRES ONLY A REASONABLE EXPECTATION OF SUCCESS

The prior art can be modified or combined to reject claims as prima facie obvious as

long as there is a reasonable expectation of success. In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986) (Claims directed to a method of treating depression with amitriptyline (or nontoxic salts thereof) were rejected as prima facie obvious over prior art disclosures that amitriptyline is a compound known to possess psychotropic properties and that imipramine is a structurally similar psychotropic compound known to possess antidepressive properties, in view of prior art suggesting the aforementioned compounds would be expected to have similar activity because the structural difference between the compounds involves a known bioisosteric replacement and because a research paper comparing the pharmacological properties of these two compounds suggested clinical testing of amitriptyline as an antidepressant. The court sustained the rejection, finding that the teachings of the prior art provide a sufficient basis for a reasonable expectation of success.); Ex parte Blanc, 13 USPQ2d 1383 (Bd. Pat. App. & Inter. 1989.

The examiner maintains that because the Cysteine rich repeats were identified as being involved in ligand binding, one of skill in the art would have a reasonable expectation that portions of TACI comprising the extracellular cysteine-rich repeat, or BCMA comprising the extracellular cysteine-rich repeat would retain the ability to bind to the TNF receptor.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Karen A. Canella, Ph.D.
12/26/2006

KAREN A. CANELLA PH.D
PRIMARY EXAMINER